measurement;

clinical chemistry instrumentation that allows automatic execution of a clinical chemistry assay measurement;

a sample handling device coupled between said immunoassay instrumentation and said clinical chemistry instrumentation to allow sharing of samples therebetween;

a computer-readable medium that stores information that represents the reflex algorithm; and

a processor coupled to said immunoassay instrumentation, said clinical chemistry instrumentation, and said computer-readable medium, wherein said processor receives information [concerning] representative of outputs from biochemical marker measurements conducted on the immunoassay instrumentation and on the clinical chemistry instrumentation, and selectively commands said immunoassay instrumentation and said clinical chemistry instrumentation to execute [a] the biochemical marker measurement according to the reflex algorithm.

11. (Amended) The system according to claim 10, wherein said processor selectively [suggests] provides a suggested [an] indication of a pathology according to the reflex algorithm in response to receiving the information [concerning] representative of outputs from biochemical marker measurements.

12. (Amended) The system according to claim 10, wherein said immunoassay instrumentation and said clinical chemistry instrumentation [each includes a respective] include a first processor and a second processor, respectively, the first and second processors capable of communicating [in communication] with said processor.

REMARKS

I. Introduction – Claim Status

This amendment under 37 C.F.R. §§1.111 is submitted in response to the outstanding Office Action of November 9, 1999, and is accompanied by a Petition for Extension of Time with fee. The Office Action indicates that claims 1-12 are now pending, and claims 13-21 are withdrawn from further consideration, in view of a Final Restriction Requirement set forth in the Office Action. Applicant hereinbelow respectfully submits that the Final Restriction Requirement is improper and thus, that claims 13-21 should also be subject to consideration on the merits. In the present amendment, claims 1 and 7-12 are herein amended for additional clarity. Applicant respectfully requests reconsideration in view of the herewith presented amendments and remarks.

II. The Final Restriction Requirement

In view of Applicant's 9/27/99 response, the 6/23/99 restriction requirement has been withdrawn; however, in the outstanding Office Action restriction under 35 U.S.C., §121 is now required to one of the following inventions:

I. Claims 1-12, drawn to a diagnostic system comprising different analyzers for performing biological marker measurements, classified in class 422, for example.

II. Claims 13-15, drawn to a computer program and computer readable medium, classified in class 266, subclass 80, for example.

III. Claims 16-21, drawn to method of using automated diagnostic system and apparatus, classified in 128, subclass 632, for example.

This restriction requirement has been made FINAL, and Group I has been examined on the merits based on Applicant's previous election with traverse.

Applicant, however, respectfully submits that this Final Restriction Requirement is improper and should be withdrawn for reasons elaborated in Applicant's 9/27/99 response to the original restriction requirement (emphasis added):

> [T]o the extent that a proper restriction requirement *has been or will be* made, however, Applicant respectfully traverses such requirement on the grounds that the inventions are obvious over each other within the meaning of 35 USC § 103. Accordingly, as indicated in MPEP §803, restriction should not be required. *In re Lee*, 199 USPQ 108 (Comm'r Pat. 1978).

In view of the foregoing, Applicant respectfully requests that the requirement for restriction be withdrawn and that claims 13-21 also be considered on the merits.

III. The 35 U.S.C. §112, ¶2 Rejections

Claims 1-12 are rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Office Action identifies specific language believed to render the claims indefinite.

Regarding claims 1 and 8-12, Applicant respectfully submits that the herein clarifying amendments of these claims has obviated and rendered moot the §112, ¶2 rejections, which should thus be withdrawn.

Regarding claim 7, the Office Action asserts that (i) "wherein the diagnosis of the pathology for the subject is based, at least in part, on results from the measurements executed according to said reflex algorithm" is indefinite because it does not specifically define what is encompassed by the recitation of "at least in part", i.e., abnormal results or elevated results, etc., and (ii) "additional stored information" renders the claim indefinite because the claim includes

elements not actually disclosed (those encompassed by "additional"), thereby rendering the scope of the claim unascertainable.

Applicants respectfully traverse this rejection on the grounds that the use of the terminology "at least in part" is not indefinite to an ordinarily skilled artisan in light of the claim language itself or further in light of the specification. The claim language plainly means that the "results from the measurements executed according to said reflex algorithm and . . . additional stored information concerning the subject" contribute to the "diagnosis of the pathology", but that this "diagnosis" is not necessarily exclusively based on the "results from the measurements executed according to said reflex algorithm and . . . additional stored information concerning the subject". Applicant submits that one skilled in the art understands that any of myriad other factors (e.g., family history, other test results, etc., preferably stored in a database) may factor into a diagnosis. Thus, there is no necessity for specifically defining what these other factors may include. Additionally, however, the specification further elaborates illustrative examples of other information that may factor into a diagnosis (see, e.g.,, p. 14, ll. 1-6), from which an ordinarily skilled artisan may further understand the meaning of the identified claim language and thus of the claim scope.

Applicant further submits that claims 1 and 8 provide cooperative relationships among the elements such that these claims are clear and unambiguous to one of ordinary skill in the art.

In view of the foregoing, Applicants respectfully submit that the rejections under 35 U.S.C. §112, second paragraph, should be withdrawn.

IV. The 35 U.S.C. §112, ¶1 Rejections

The Office Action states that claims 1-12 are rejected under 35 USC 112, first paragraph, because the specification, while being enabling for acute myocardial infarction biochemical markers, does not reasonably provide enablement for other biochemical markers, such as thyroid profile markers and hepatitis profile markers. It further asserts that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. More specifically, the Office Action sets forth the following reasoning:

> As to the biochemical markers, the direction and guidance in the specification is notably limited to specific acute myocardial infarction markers, such as total creatine kinase, myoglobin, troponin I, etc. The working examples, likewise are limited to the cardiac markers. Based on this limited disclosure and direction, one of the skill in the art would not know ho to use alternative biochemical markers, such as thyroid profile markers in the instant diagnostic system which comprise immunoassay analyzer, clinical chemistry analyzer, and hematology analyzer, with undue experimentation.

Applicant respectfully submits that the specification clearly and completely describes the invention such that an ordinarily skilled artisan would know how to make and/or use the claimed invention without undue experimentation. That is, an ordinarily skilled artisan would know how to make and use Applicant's claimed invention (e.g., claim 1) such that the program would implement any reflex algorithm that may be developed and which includes both immunoassays and clinical chemistry assays to diagnose pathology. Accordingly, Applicant submits that the specification clearly enables the claimed invention, and thus requests withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

Additionally, in the Office Action claim 9 is rejected under 35 USC 112, first paragraph, because the specification, while being enabling for automated immunoassay analyzers and clinical chemistry analyzers, allegedly does not reasonably provide enablement for other assay means for performing measurements, such as individual assay kit means and manually programmed assay means. It is asserted that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. More specifically, the reasoning set forth in the Office Action is as follows:

> As to the assay means for performing biochemical marker measurements, the direction and guidance in the specification is notably limited to automated analyzers and processors, etc. The working examples, likewise are limited to the automated biochemical assays. Based on this limited disclosure and direction, one of the skill in the art would not know how to use alternative means of measuring such as assay kits, means of processing information such as visual interpretation of a reaction, and means for storing information, such as record keeping, in the instant diagnostic system, without undue experimentation.

Applicant respectfully traverses this rejection and requests that it be withdrawn. Claim 9 is set forth as a means-plus-function claim directed to corresponding *structure* disclosed in the specification and equivalents thereof. As the specification clearly describes many illustrative processor controlled reflex algorithm implementations of immunoassays and clinical chemistry measurements, Applicant respectfully submits that one of ordinary skill in the art would know how to make and/or use alternative processor based implementations, without limiting each and every element to being completely automated. For example, certain kits may include both manual and automated steps. Accordingly, Applicant submits that the specification reasonably enables implementing invention of claim 9 for other assay means that are not

completely automated, and thus requests withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

V. The 35 U.S.C. §103(a) Rejections

Claims 1-12 have been rejected under 35 USC 103(a) as being unpatentable over Lillig et al. (US 4,965,049) in view of Groth et al. (US 5,690,103) and in further view of Furlong et al. (Clinical Chemistry, 1990).

More specifically, the Office Action states the following (emphasis added):

> Lillig et al. disclose a system of modular analyzers each adapted for independent operation and each possessing different operational characteristics for different applications (see Abstract). *The system includes at least a first analyzer, i.e., immunoassay and a second analyzer, i.e., clinical chemistry,* each including a sample carousel, analyzing means, and automated probe means for transferring samples from the sampling carousels to the analyzing means. . . .
>
> Lillig et al. differs in failing to teach diagnostic nature of the modular analyzer system. Lillig et al. are silent in the teaching of analyte assays and thereby, fail to disclose analysis of biochemical markers.
>
> Groth et al. disclose detection or exclusion of acute myocardial infarction (AMI) *using reflex algorithm (computer based neural network analysis)* in biochemical marker measurements. Groth et al. specifically disclose diagnostic categorization of AMI based on frequent timed blood sampling and measurement of selected biochemical markers with different rates of appearance in circulating blood (see Abstract). *Reflex algorithm or neural network is a computational structure which is trained on a representative set of preclassified example cases, prior to application in unknown cases.* . . .
>
> Furlong et al. teach a diagnostic system based on *reflex algorithm (computerized neural network analysis)* of serial cardiac enzyme data for use as clinical decision-making aid (see Abstract). Neural networks are hardware and software emulations of biological nervous systems, formed by many interconnected artificial neurons (see page 135, column 1, first full paragraph). Furlong et al. studies criteria for diagnosing acute myocardial

> infarct using biochemical markers (cardiac enzymes) as listed in Table 1 and column 1 and applies it in neural network design. . . .
>
> It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate *computer-based neural network analysis* as taught by Groth et al. and Furlong et al. into the modular analyzer system as taught by Lillig et al. because Groth et al. specifically disclose application of his teaching into decentralized analyzers in order to expedite analysis of patient samples in emergency situations and Furlong et al. specifically teaches that the neural network has proven to be useful adjunct to traditional methods.

Applicant respectfully disagrees and traverses this rejection on the grounds, inter alia, that even assuming arguendo that there is a motivation or suggestion for combining Lillig, Groth, and Furlong, such a combination fails to teach or suggest Applicant's claimed invention.

As may be appreciated, Applicant's claimed invention (claim 1) is directed to a diagnostic system that includes an immunoassay analyzer, a clinical chemistry analyzer, and an automatic sample handling device coupled between the immunoassay analyzer and the clinical chemistry analyzer to allow sharing of samples therebetween. A processor communicates with the immunoassay analyzer and the clinical chemistry analyzer, wherein the processor commands the immunoassay analyzer and clinical chemistry analyzer to execute measurements specified by a program executed by the processor in order to facilitate diagnosis of a pathology for a subject according to a reflex algorithm which includes at least one immunoassay and at least one clinical chemistry assay. Additionally, Applicant's invention of claim 9 is directed to a system for executing a sequence of biochemical marker measurement steps, including immunoassay and clinical chemistry assay measurements, to generate an indication of a pathology, the system including means for selectively commanding an immunoassay measurement means and a clinical chemistry assay means to perform specified biochemical marker measurements according to a

reflex algorithm.

Applicant respectfully submits that Lillig, Groth, and Furlong, individually and in combination, do not teach or suggest, *inter alia*, a system that includes an immunoassay analyzer and a clinical chemistry assay analyzer that are controlled according to "reflex algorithm", as claimed by Applicant. As understood by those skilled in the art, and as explained in Applicant's specification (see, e.g., p. 2, l. 14 et seq.), a reflex algorithm refers to an algorithm in which the selection/performance of a subsequent test is based on results of previous tests, without the need for subjective human decision-making in selecting tests.

Consonant with the Examiner's statement that Lillig et al. "fail[] to teach diagnostic nature of the modular analyzer system. . . . [and] are silent in the teaching of analyte assays and thereby, fail to disclose analysis of biochemical markers", Applicant submits that the Lillig et al reference relates to a modular clinical chemistry analyzer and neither discloses nor suggests performing tests on the modular analyzer according to a "reflex algorithm". (Applicant also submits that, contrary to the Office Action, Lillig does not describe immunoassay tests, but only describes clinical chemistry tests; nevertheless, Lillig doesn't teach or suggest performing tests based on a "reflex algorithm").

Groth relates to neural network analysis of biochemical marker measurements to classify patients suspected of having acute myocardial infarction (AMI). Such neural network analysis provides classification based on inputs from results of a set of biochemical marker measurements taken at certain time intervals. The neural network has been previously trained based on a training sample set, and the results of the biochemical marker measurements are input into the neural network, which then outputs an indication of AMI. This neural network paradigm

is in stark contrast to a reflex algorithm as claimed by Applicant's, at least to the extent that the neural network classifies according to a predetermined set of biochemical marker measurements (the results of which are all input into the neural network). In contradistinction, in a reflex algorithm which (if any) subsequent biochemical marker measurement is performed depends upon the results of previous measurements, and the indication and sequence of tests performed are thus inter-related. (Applicant respectfully notes that the background section of Applicants' specification provides additional background explanation of neural network techniques and reflex algorithm techniques.)

Furlong, like Groth, relates to a neural network analysis of biochemical markers for detecting AMI and thus, based on similar reasoning, does not teach or suggest a system that includes immunoassays and clinical chemistry assays executed according to a "reflex algorithm".

Thus, for at least these reasons, Applicants respectfully submit that even assuming arguendo that Lillig, Groth, and Furlong may be combined as asserted in the Office Action, such a combination would fail to teach or suggest all the limitations of Applicant's claimed invention. Accordingly, Applicant respectfully requests that the §103(a) rejection of claims 1-12 be withdrawn.

VI. Conclusion

In view of the above amendments and remarks, Applicants respectfully submit that the application is in condition for allowance. Reconsideration and withdrawal of the Examiner's rejections is respectfully requested and allowance of all pending claims is respectfully submitted.

If any outstanding issues remain, or if the Examiner has any suggestions for expediting allowance of this application, the Examiner is invited to contact the undersigned at the telephone number below.

The Examiner's consideration of this matter is gratefully acknowledged.

Respectfully submitted,

MORGAN & FINNEGAN

Date: May 9, 2000 By: _____

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